

PHASE I TRIAL REPRESENTATION AND GEOGRAPHIC DISTRIBUTION IN MESOTHELIOMA AND THYMIC EPITHELIAL TUMORS

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Background

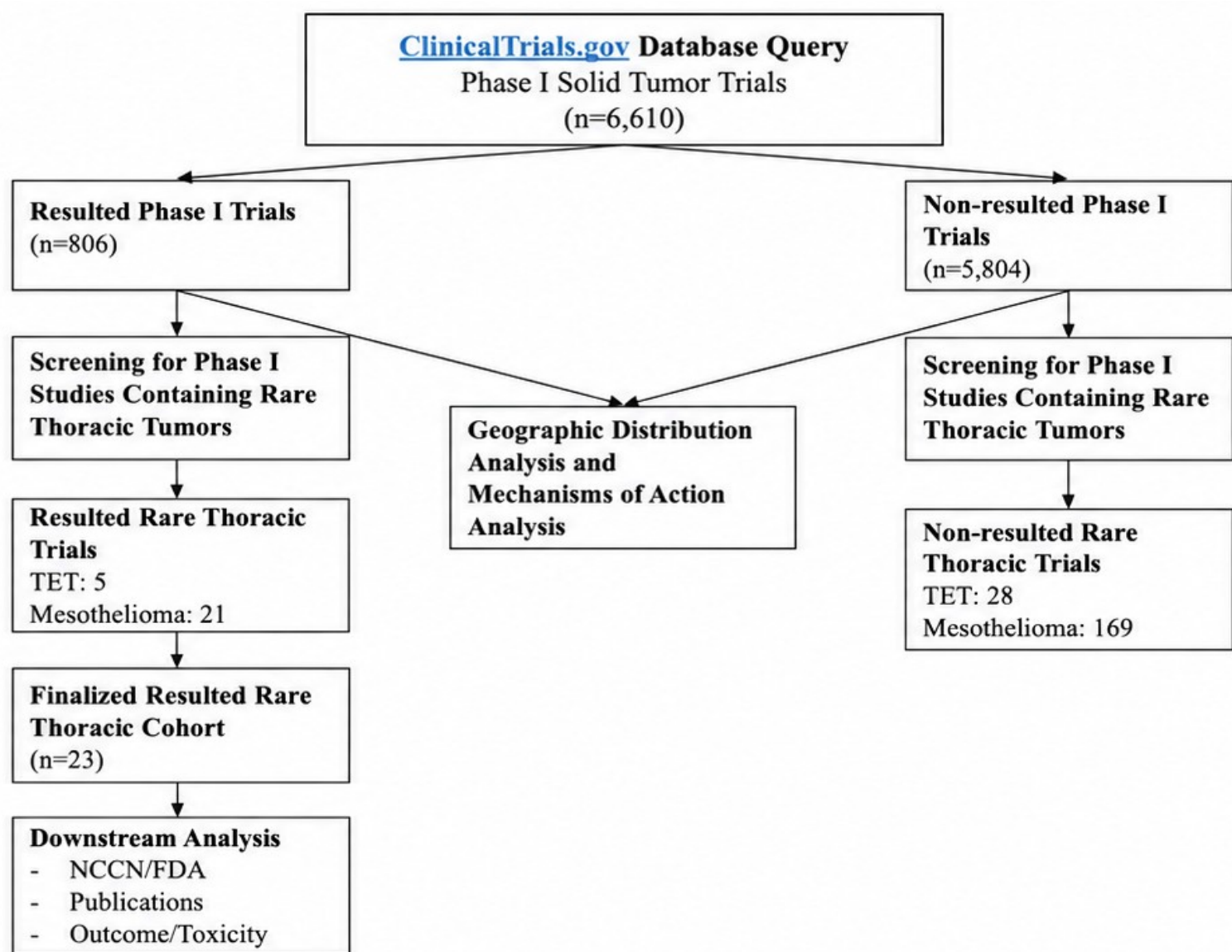
Rare thoracic malignancies, including malignant pleural mesothelioma and thymic epithelial tumors (TETs), face poor prognoses and underrepresentation in clinical trials.

To characterize, the early-phase therapeutic landscape and global access disparities, we evaluated the representation, geographic distribution, mechanisms of action, and translational outcomes of Phase I solid tumor trials on ClinicalTrials.gov (1995-2026).

Methods

Phase I solid-tumor trials (1995-2026) were queried from ClinicalTrials.gov (N=6,610) using a python pipeline, identifying 23 resulted and 197 non-resulted trials permitting mesothelioma or TETs.

We extracted mechanisms of action, geographic trial locations, clinical endpoints, FDA/NCCN translation, and peer-reviewed publication rates across the resulted cohort.



Result

Fig-1: Representation of TETs and mesothelioma among resulted (A; n=806) and non-resulted (B; n=5,804) Phase I solid tumor trials

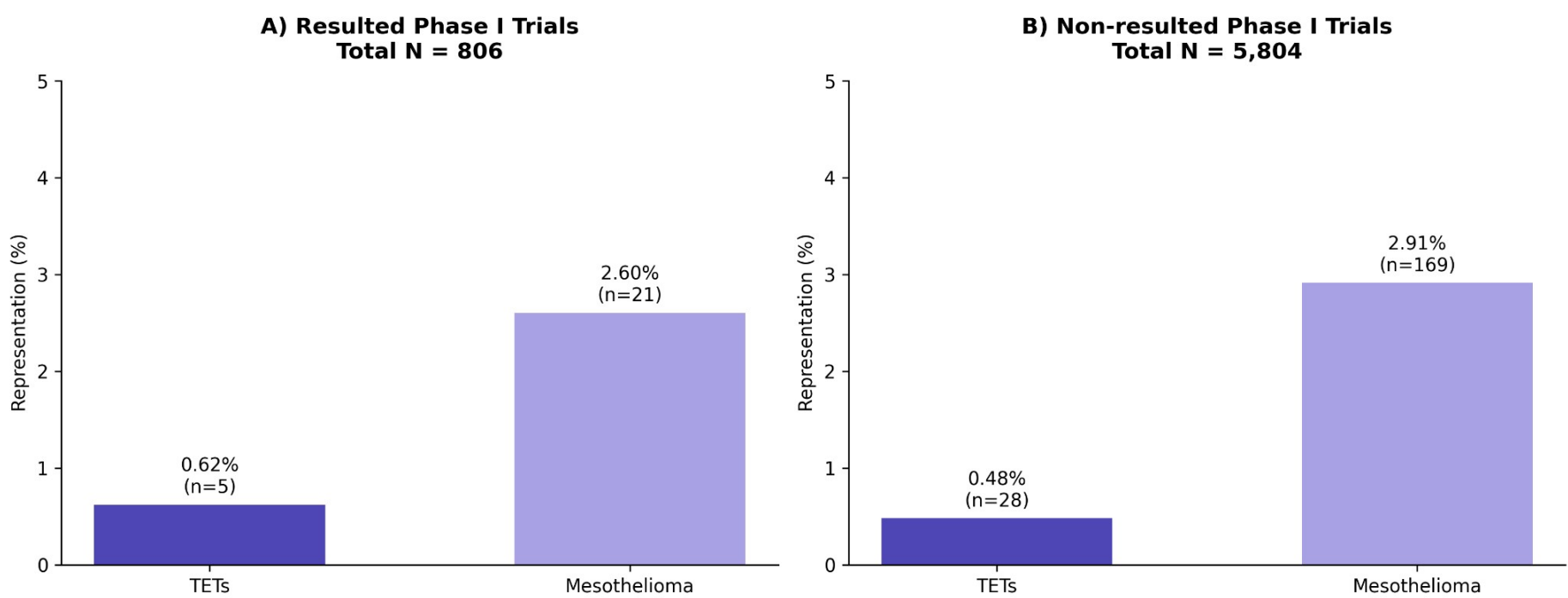


Fig-2: World map depicting the geographic distribution of trial locations among resulted Phase I trials enrolling patients with mesothelioma and TETs

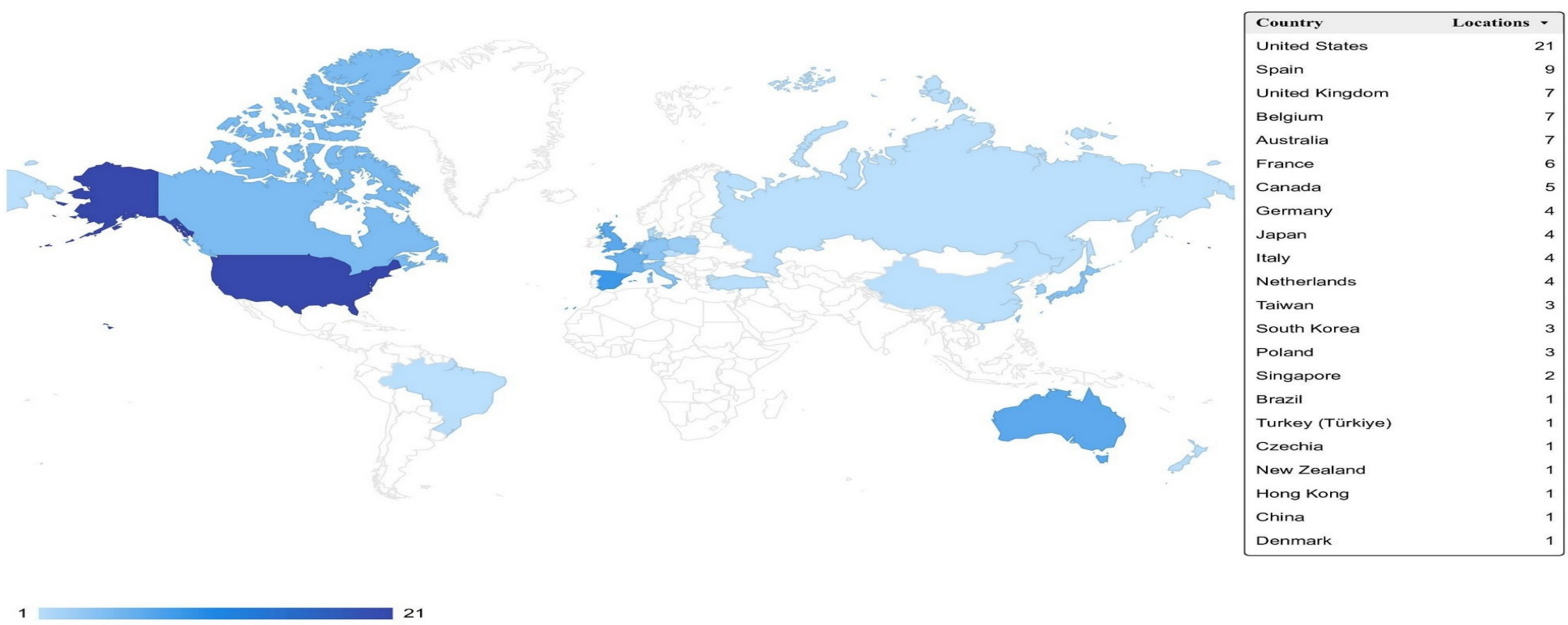


Fig-3: Summary of toxicity profiles and clinical outcomes by therapeutic class in resulted Phase I rare thoracic malignancy trials

Therapy Type	Most Common Toxicities (top 3, % of studies)	≥ Grade 3 Toxicity (%)	ORR (%)	PFS (months)	OS (months)
Targeted Therapy (n=12)	1. Fatigue (58%) 2. Gastrointestinal toxicity (58%) 3. Hematologic toxicity (42%)	0–51.7	0–44.0	1.8–6.6	3.0–15.9
Immunotherapy (n=6)	1. Fatigue (100%) 2. Gastrointestinal toxicity (83%) 3. Dermatologic toxicity (50%)	5–27	9.0–29.0	1.6–6.3	6.0–12.5
Immune + Targeted (n=2)	1. Immune-related toxicities (100%) 2. Capillary leak syndrome/edema (100%) 3. Infusion reactions (50%)	19–61.7	0–20.0	1.3–8.3	3.4–19.3
ADC (n=2)	1. Fatigue (100%) 2. Nausea (100%) 3. Peripheral edema/neuropathy (50%)	25–49	≥6.0 (upper bound NR)	NR	NR

Table 1. FDA Approval and NCCN Guideline Inclusion of Therapeutic Agents Identified in Resulted Mesothelioma and Thymic Epithelial Tumor (TET) Phase I Clinical Trials

Classification	Mesothelioma (n = 32)	TET (n = 10)
FDA-approved and/or NCCN-included for disease	5 (15.6%)	2 (20.0%)
FDA-approved for other indications but not disease-specific	9 (28.1%)	3 (30.0%)
Neither FDA-approved nor NCCN-included	18 (56.3%)	5 (50.0%)
Total	32 (100%)	10 (100%)

Summary

- ❑ Rare thoracic tumors comprised only **2.85%** of resulted Phase I solid tumor trials
- ❑ Trial activity was heavily concentrated in **Europe (49.0%)** and the **US (21.9%)**.
- ❑ **Targeted therapies (65.2%)** and **immunotherapies (34.8%)** were the predominant investigational classes.
- ❑ **0% of novel agents** achieved disease-specific FDA approval or NCCN inclusion.
- ❑ **43.5%** of resulted trials remained **unpublished** in peer-reviewed literature.
- ❑ Overall response rates ranged from **0–44%** with median PFS remaining **<9 months** across all therapeutic classes.

Future Directions

Expand Global Infrastructure: Establish early-phase trial networks in historically underrepresented regions to improve geographic diversity and equitable therapeutic access.

Diversify Therapeutic Modalities: Accelerate investigation beyond standard targeted therapies by expanding early-phase evaluation of antibody-drug conjugates (ADCs), bispecific, and novel immunotherapies.

Improve Dissemination: Encourage peer-reviewed publication of all completed Phase I trials to mitigate reporting bias in rare diseases.